

**INTERNATIONAL SEARCH AUTHORITY
EUROPEAN PATENT OFFICE, THE HAGUE**

Applicant :CASE WESTERN RESERVE UNIVERSITY
International Application No. :PCT/IB2005/050257
International Filing Date :January 21, 2005
Priority Date Claimed :January 21, 2004
Title :Hybrid and Chimeric Polypeptides that
Regulate Activation of Complement
Authorized Officer :Ismail Abdulaziz

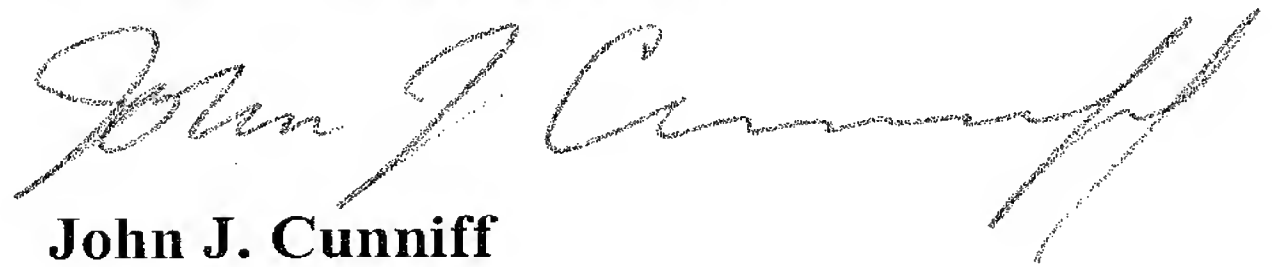
RESPONSE TO INVITATION TO CORRECT DEFECTS

Dear Sir or Madam:

In response to the Invitation to Correct Defects (Form PCT/RO/106) dated 2 February 2005, the Applicants, through their attorney, provide herewith replacement pages 34-36.

If the Authorized Officer should have any questions or wish to discuss any aspect of this Response to the Invitation to Correct Defects, the undersigned would welcome a telephone call from the Authorized Officer.

Respectfully submitted,



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result is shown in Fig. 22, where DAF-CR1B acts as cofactor for factor I as shown by the appearance of a band at 29 kDa.

[00143] Based upon the foregoing disclosure, it should be apparent that the present invention will carry out the aspects set forth above. It is therefore, to be understood that any variations evident fall within the scope of the invention and thus, the selection of specific component elements can be determined without departing from the spirit of the invention herein disclosed and described.

CLAIMS

We claim:

1. A protein comprising:

a first functional unit of a first complement regulatory protein, wherein the first functional unit exhibits complement-regulating properties;

a first spacer sequence of at least about 200 amino acids encoding a polypeptide that does not exhibit complement regulating properties, attached to the first functional unit; and

a second functional unit attached to the spacer sequence, selected from the group consisting of polypeptides providing a functional unit of a second complement regulatory protein, polypeptides derived from an immunoglobulin, and polypeptides that enhance binding of the protein to an animal cell.

2. The protein of claim 1, additionally comprising a second spacer sequence of at least about 200 amino acids encoding a polypeptide that does not exhibit complement regulating properties attached to the second function domain, and a third functional unit attached to the second spacer, wherein the third functional unit is selected from the group consisting of polypeptides derived from an immunoglobulin, and polypeptides that enhance binding of the protein to an animal cell.

3. The protein of claim 1, wherein the first functional unit comprises at least CCPs 2, 3 and 4 of DAF.

4. The protein of claim 1, wherein the second functional unit is selected from the group consisting of CCPs 8-10 of Complement Receptor 1 (CR1), CCPs 15-17 of CR1, CCPs 1-4 of Membrane Cofactor Protein (MCP), polypeptides derived from IgG4, and a lipid tail.

5. The protein of any of claims 1-4, wherein the spacers are selected from the group consisting of substantially all of the amino acids of CCPs 4-7 of CR1, and substantially all of the amino acids of CCPs 11-14 of CR1.

6. The protein of claim 1, wherein the first functional unit comprises CCPs 1, 2, 3 and 4 of DAF, the second functional unit is selected from the group consisting of CCPs 8-10 of CR1, CCPs 1-4 of Membrane Cofactor Protein (MCP), and polypeptides derived from IgG4, and the first spacer is substantially all of the amino acids of CCPs 4-7 of CR1.
7. The protein of claim 6, additionally comprising a second spacer comprising substantially all of the amino acids of CCPs 4-5 of CR1, and a third functional unit selected from the group consisting of CCPs 8-10 of CR1 CCPs 1-4 of MCP, and polypeptides derived from Ig G4.
8. A polynucleotide encoding the protein of claim 6.
9. A polynucleotide encoding the protein of claim 7.
10. A polynucleotide encoding the protein of claim 1.
11. A vector comprising the polynucleotide of claim 10.
12. A protein having at least 95 percent sequence homology to a protein selected from the group consisting of proteins having the sequence of SEQ. ID NO: 13, SEQ. ID NO: 15, SEQ. ID NO: 19, and SEQ. ID NO: 23.
13. A polynucleotide encoding the protein of claim 11.
14. A method of regulating complement activity comprising administering an effective amount of protein of claim 1 to a mammal.
15. The method of claim 15, wherein the mammal is a human.